

CLAIMS

What is claimed is:

1. A method for screening a compound, wherein the method comprises:
  - (a) contacting the compound with a cell, wherein the cell comprises:
    - 5 (i) a first polynucleotide encoding a protein comprising a fusion between a first functional domain and a first engineered zinc finger protein targeted to a first endogenous cellular gene; and
    - (ii) a second polynucleotide encoding a protein comprising a fusion between a second functional domain and a second engineered zinc finger protein  
10 targeted to a second endogenous cellular gene; and
  - (b) measuring expression of the first and second endogenous genes.
2. The method of claim 1, wherein the first functional domain is a drug target or a functional fragment thereof.
3. The method of claim 2, wherein the second functional domain is a drug  
15 target or functional fragment thereof.
4. The method of claim 3, wherein the first and second functional domains are from the same drug target.
5. The method of claim 3, wherein the first and second functional domains are from different drug targets.
- 20 6. The method of claim 2, wherein the second functional domain is a protein related to the drug target or a functional fragment thereof.
7. The method of claim 2, wherein the second functional domain is a xenobiotic receptor or a functional fragment thereof.
8. The method of claim 2, wherein the second functional domain is a  
25 molecule involved in drug metabolism or a functional fragment thereof.
9. The method of claim 1, wherein the first functional domain is a hormone receptor, an orphan receptor, or a functional fragment thereof.

10. The method of claim 1, wherein the first polynucleotide is stably integrated into the chromosome of the cell.

11. The method of claim 10, wherein the second polynucleotide is stably integrated into the chromosome of the cell.

5 12. The method of claim 1, wherein the cell is a mammalian cell.

13. The method of claim 1, wherein expression of the endogenous genes is measured by assaying RNA levels.

14. The method of claim 1, wherein expression of the endogenous genes is measured by assaying protein levels.

10 15. The method of claim 1, wherein expression of the endogenous genes is measured by assaying enzymatic activity of the gene products.

16. The method of claim 1, wherein expression of the first endogenous gene is activated by the first functional domain.

15 17. The method of claim 1, wherein expression of the first endogenous gene is repressed by the first functional domain.

18. The method of claim 1, wherein the compound is screened for specificity.

19. The method of claim 1, wherein the compound is screened for toxicity.

20. The method of claim 1, wherein the compound is screened for its metabolic properties.

20 21. A cell comprising:

(a) a first polynucleotide encoding a protein comprising a fusion between a first functional domain and a first engineered zinc finger protein targeted to a first endogenous cellular gene; and

25 (b) a second polynucleotide encoding a protein comprising a fusion between a second functional domain and a second engineered zinc finger protein targeted to a second endogenous cellular gene.

22. The cell of claim 21, wherein the first functional domain is a drug target or a functional fragment thereof.

23. The cell of claim 22, wherein the second functional domain is a drug target or functional fragment thereof.

5 24. The cell of claim 23, wherein the first and second functional domains are from the same drug target.

25. The method of claim 23, wherein the first and second functional domains are from different drug targets.

10 26. The cell of claim 22, wherein the second functional domain is a protein related to the drug target or a functional fragment thereof.

27. The cell of claim 22, wherein the second functional domain is a xenobiotic receptor or a functional fragment thereof.

28. The cell of claim 22, wherein the second functional domain is a molecule involved in drug metabolism or a functional fragment thereof.

15 29. The cell of claim 21, wherein the first functional domain is a hormone receptor, an orphan receptor, or a functional fragment thereof.

30. The cell of claim 21, wherein the first polynucleotide is stably integrated into the chromosome of the cell.

20 31. The cell of claim 30, wherein the second polynucleotide is stably integrated into the chromosome of the cell.

32. The cell of claim 21, wherein the cell is a mammalian cell.

33. The cell of claim 21, further comprising a third polynucleotide encoding a protein comprising a fusion between a third functional domain and a third engineered zinc finger protein targeted to a third endogenous cellular gene.

25 34. The cell of claim 33, further comprising a fourth polynucleotide encoding a protein comprising a fusion between a fourth functional domain and a fourth engineered zinc finger protein targeted to a fourth endogenous cellular gene.

**35.** The cell of claim 34, further comprising a fifth polynucleotide encoding a protein comprising a fusion between a fifth functional domain and a fifth engineered zinc finger protein targeted to a fifth endogenous cellular gene.